

Applicant : Ilya Trakht et al.
Serial No.: 09/664,958
Filed: September 18, 2000
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Amendments to the Specification:

Please amend the specification under the provisions of revised 37 C.F.R. §1.121 as indicated below, with deleted matter indicated by strikethrough and added matter indicated by underlining.

On page 20, please replace the paragraphs between lines 25-31 with the following amended paragraphs:

-- The present invention provides an isolated peptide having the amino acid sequence Lys Leu Leu Gly Gly Gln Ile Gly Leu ~~(SEQ. ID No.)~~ (SEQ ID No:3).

D¹
The present invention provides an isolated peptide having the amino acid sequence Ser Leu Leu Gly Cys Arg His Tyr Glu Val ~~(SEQ. ID No.)~~ (SEQ ID NO:4). --

Please replace the paragraphs between page 25, line 37 and page 26, line 30 with the following amended paragraphs:

D²
-- The present invention provides a method for diagnosing cancer associated with the expression of TIP-2 antigen in a human subject which comprises: (a) obtaining mRNA from a sample of the subject's peripheral blood; (b) preparing cDNA from the mRNA from step (a); (c) amplifying DNA encoding TIP-2 antigen present in the cDNA prepared in step (b) by a polymerase chain reaction utilizing at least two oligonucleotide primers, wherein each of the primers specifically hybridizes with DNA encoding TIP-2 antigen, wherein the primers comprise oligonucleotides having a sequence included within the sequence of ~~SEQ ID NO.~~ SEQ ID NO:2; and (d) detecting the presence of any resulting

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amplified DNA, the presence of such amplified DNA being diagnostic for cancer associated with the expression of TIP-2 antigen.

The present invention provides a method for diagnosing cancer associated with the expression of TIP-2 antigen in a human subject which comprises: (a) obtaining mRNA from a sample of the subject's peripheral blood; (b) preparing cDNA from the mRNA from step (a); (c) amplifying DNA encoding TIP-2 antigen present in the cDNA prepared in step (b) by a polymerase chain reaction utilizing at least two oligonucleotide primers, wherein each of the primers specifically hybridizes with DNA encoding TIP-2 antigen, wherein the primers comprise oligonucleotides having a sequence included within the sequence of ~~SEQ ID NO. 1~~ SEQ ID NO:2; and (d) determining the amount of any resulting amplified DNA; and (e) comparing the amount of amplified DNA determined in step (d) with previously determined standard amounts of amplified DNA, each standard amount being indicative of a particular stage of cancer associated with the expression of TIP-2 antigen. --

On pages 33-35, please amend the brief descriptions of Figures 29, 30 and 32-42 as follows:

Figure 29

D3
The amino acid sequence (SEQ ID NO:1) of GIPC/TIP-2 protein. In italics, the amino acid sequence of TIP-2 only. Underlined are two peptides identified as high HLA-*A0201 binders (theoretical calculation).

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Figure 30

The mRNA sequence (SEQ ID NO:2) of GIPC. The part of the sequence corresponding to TIP-2 is underlined.

Figure 32

Human mRNA sequence for KIAA0338 gene, partial cds (SEQ ID NO:5) and sequence of translation product (SEQ ID NO:6).

Figure 33

Human non-muscle alpha-actinin mRNA sequence, complete cds (SEQ ID NO:7) - the second non-muscle alpha-actinin isoform designated ACTN4 (actinin-4), and sequence of translation product (SEQ ID NO:8).

Figure 34

Homo sapiens actinin, alpha 4 (ACTN4) mRNA sequence (SEQ ID NO:9) and sequence of translation product (SEQ ID NO:10).

Figure 35

Clathrin coat assembly protein AP50 mRNA sequence (SEQ ID NO:11) and sequence of translation product (SEQ ID NO:12).

Figure 36

Homo sapiens GLUT1 C-terminal Binding protein (GLUT1CBP) mRNA sequence (SEQ ID NO:13) and sequence of translation product (SEQ ID NO:14).

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Figure 37

gp130 associated protein GAM sequence (SEQ ID NO:15) and
sequence of translation product (SEQ ID NO:16).

Figure 38

Homo sapiens amino-terminal enhancer of split (AES) mRNA
sequence (SEQ ID NO:17) and sequence of translation product
(SEQ ID NO:18).

Figure 39

Antiquitin 1 (antiquitin=26g turgor protein homolog), mRNA
sequence (SEQ ID NO:19) and sequence of translation product
(SEQ ID NO:20).

Figure 40

ARP2/3 protein complex 41 KD subunit (P41-ARC), mRNA
sequence (SEQ ID NO:21) and sequence of translation product
(SEQ ID NO:22).

Figure 41a

H. sapiens seb4D mRNA sequence (SEQ ID NO:23) and sequence
of translation product (SEQ ID NO:24).

Figure 41b

H. sapiens seb4B mRNA sequence (SEQ ID NO:25) and sequence
of translation product (SEQ ID NO:26).

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Figure 42

Homo sapiens lamin A/C (LMNA) mRNA sequence (SEQ ID NO:27)
and sequence of translation product (SEQ ID NO:28).

On page 79, please replace the paragraphs between lines 5-11 with the following amended paragraphs:

-- In an embodiment of this invention the peptide fragment of TIP-2 antigen comprises the amino acid sequence Lys Leu Leu Gly Gly Gln Ile Gly Leu (~~SEQ. ID NO.~~) (SEQ ID NO:3).

D5 In an embodiment of this invention the peptide fragment of TIP-2 antigen comprises the amino acid sequence Ser Leu Leu Gly Cys Arg His Tyr Glu Val (~~SEQ. ID No.~~) (SEQ ID NO:4). --

On the same page 79, please replace the paragraphs between lines 31-37 with the following amended paragraphs:

-- In an embodiment of this invention the peptide fragment of TIP-2 antigen comprises the amino acid sequence Lys Leu Leu Gly Gly Gln Ile Gly Leu (~~SEQ. ID NO.~~) (SEQ ID NO:3).

D6 In an embodiment of this invention the peptide fragment of TIP-2 antigen comprises the amino acid sequence Ser Leu Leu Gly Cys Arg His Tyr Glu Val (~~SEQ. ID No.~~) (SEQ ID NO:4). --

On page 81, please replace the paragraphs between lines 4-10 with the following amended paragraphs:

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-- The present invention provides an isolated peptide having the amino acid sequence Lys Leu Leu Gly Gly Gln Ile Gly Leu (~~SEQ. ID No.~~) (SEQ ID NO:3).

D7
The present invention provides an isolated peptide having the amino acid sequence Ser Leu Leu Gly Cys Arg His Tyr Glu Val (~~SEQ. ID No.~~) (SEQ ID NO:4). --

Please replace the paragraphs between page 93, line 29 and page 94, line 16 with the following amended paragraphs:

D8
-- The present invention provides a method for diagnosing cancer associated with the expression of TIP-2 antigen in a human subject which comprises: (a) obtaining mRNA from a sample of the subject's peripheral blood; (b) preparing cDNA from the mRNA from step (a); (c) amplifying DNA encoding TIP-2 antigen present in the cDNA prepared in step (b) by a polymerase chain reaction utilizing at least two oligonucleotide primers, wherein each of the primers specifically hybridizes with DNA encoding TIP-2 antigen, wherein the primers comprise oligonucleotides having a sequence included within the sequence of ~~SEQ ID NO.~~ SEQ ID NO:2; and (d) detecting the presence of any resulting amplified DNA, the presence of such amplified DNA being diagnostic for cancer associated with the expression of TIP-2 antigen.

In the above described method, since the nucleic acid structure of TIP-2 is known, one of skill in the art may measure the expression of TIP-2 mRNA by Northern Blot since the full mRNA sequence is known and the full size cDNA can therefore be made. Another way to measure the expression is

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by quantitative PCR using 18-21 mer primers on the basis of the known mRNA sequence. One of skill in the art may also synthesize specific primers or make the full size cDNA. The full mRNA sequence of GIPC (GAIP Interacting Protein, C terminus) is shown in Figure 24 30, with the part corresponding to TIP-2 sequence underlined. --

On page 95, please replace the paragraph between lines 22-23 with the following amended paragraph:

D⁹ -- [As used herein, "whole TIP-2 antigen protein" comprises the amino acid sequence shown in Figure 23 29 (~~SEQ ID. NO.~~
SEQ ID NO:1).] --